

WHAT IS CLAIMED:

1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:

5 an array of a plurality of oligonucleotide analogue probes having different sequences, wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations and wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets with a similar hybridization stability across the array.

10 2. The composition of claim 1, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the
15 complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.

20 3. The composition of claim 1, wherein said solid substrate is selected from the group consisting of silica, polymeric materials, glass, beads, chips, and slides.

4. The composition of claim 1, wherein said composition comprises an array of oligonucleotide analogue probes 4 to 20 nucleotides in length.

25 5. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a peptide nucleic acid.

30 6. The composition of claim 1, wherein said solid substrate is attached to over 1000 different oligonucleotide analogue probes.

35 7. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a nucleotide with a 5-propynyluracil base.

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8. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by light-directed chemical coupling.

5 9. The composition of claim 8, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.

10 10. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by flowing oligonucleotide analogue reagents over known locations of the solid substrate.

15 11. The composition of claim 10, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.

20 12. A composition for analyzing the interaction between an oligonucleotide target and an oligonucleotide probe comprising:
an array of a plurality of oligonucleotide probes having different sequences hybridized to complementary oligonucleotide analogue targets, wherein said oligonucleotide analogue targets bind to complementary oligonucleotide probes with a similar hybridization stability across the array.

25 13. The composition of claim 12, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.

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14. The composition of claim 12, wherein at least one of said plurality of oligonucleotide probes comprise at least one oligonucleotide analogue.

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15. A method of analyzing interactions between an oligonucleotide target and an oligonucleotide probe comprising the steps of:

- (a) synthesizing an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences, wherein said
- 5 oligonucleotide analogue probes are coupled to a solid substrate at known locations, said solid substrate having a surface;
- (b) exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under hybridization conditions such that said plurality of oligonucleotide analogue probes bind to complementary oligonucleotide targets with a
- 10 similar hybridization stability across the array; and
- (c) determining whether an oligonucleotide analogue probe of said oligonucleotide probe array binds to at least one of said target nucleic acids.

16. The method of claim 15, wherein at least one of said

15 oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.

17. The method of claim 15, wherein said oligonucleotide target is genomic DNA.

18. The method of claim 15, wherein said target nucleic acid is

25 amplified prior to said hybridization step.

19. The method of claim 15, wherein said plurality of oligonucleotide analogue probes is synthesized on said solid support by light-directed synthesis.

20. The method of claim 15, wherein said plurality of said oligonucleotide analogue probes is synthesized on said solid support by causing oligonucleotide analogue synthetic reagents to flow over known locations of said solid support.

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21. The method of claim 15, wherein said solid substrate is selected from the group consisting of beads, slides, and chips.

22. The method of claim 15, wherein said solid substrate is comprised
5 of materials selected from the group consisting of silica, polymers, and glass.

23. The method of claim 15, wherein the oligonucleotide analogue probes of said array are synthesized using photoremovable protecting groups.

10 24. The method of claim 15, wherein at least one of said oligonucleotide analogue probes is synthesized from phosphoramidite reagents.

25. A method of detecting an oligonucleotide target comprising:
enzymatically copying an oligonucleotide target using at least one
15 nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;
selecting said oligonucleotide analogue targets such that said
oligonucleotide analogue targets bind to the complementary oligonucleotide probes
coupled to a solid surface at known locations of an array with a similar hybridization
stability across the array;
20 hybridizing the oligonucleotide analogue targets to complementary
oligonucleotide probes; and
detecting whether at least one of said oligonucleotide analogue targets
binds to said complementary oligonucleotide acid probe.

25 26. The method of claim 25, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target
30 anneals.

27. The method of claim 25, wherein the oligonucleotide probe array comprises at least one oligonucleotide analogue probe which is complementary to at least one of said oligonucleotide analogue targets.

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28. A method of making an array of oligonucleotide probes comprising:
providing a plurality of oligonucleotide analogue probes having at least one
oligonucleotide analogue, said oligonucleotide analogue probes having different sequences
5 at known locations on an array, and

selecting the oligonucleotide analogue probes to hybridize with
complementary oligonucleotide target sequences under hybridization conditions such that
said oligonucleotide analogue probes bind to complementary oligonucleotide targets with
a similar hybridization stability across the array.

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29. The method of claim 28, wherein at least one of said
oligonucleotide analogue probes has increased the thermal stability between said
oligonucleotide analogue probe and said complementary oligonucleotide target as
compared to an oligonucleotide probe that is the perfect complement to the
15 complementary oligonucleotide target with which said oligonucleotide analogue probe
anneals.

30. The method of claim 28 further comprising:
incorporating a 5-propynyluracil base into the oligonucleotide analogue
20 probes of the array.

31. The method of claim 28 further comprising:
selecting said at least one oligonucleotide analogue such that
oligonucleotide analogue probes comprises at least one peptide nucleic acid.

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32. The method of claim 28 further comprising:
providing said plurality of oligonucleotide analogue probes in an array with
at least 1000 other oligonucleotide analogue probes.

30 33. A composition for analyzing interactions between oligonucleotide
targets and oligonucleotide probes comprising:
a solid substrate and
an array of a plurality of oligonucleotide analogue probes coupled to the
solid substrate, wherein the oligonucleotide analogue probes have different sequences and

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are selected to hybridize to complementary oligonucleotide targets under uniform hybridization conditions.

34. A composition for analyzing interactions between oligonucleotide
5 targets and oligonucleotide probes comprising:

an array of a plurality of oligonucleotide probes having different sequences hybridized to complementary oligonucleotide analogue targets, wherein the oligonucleotide analogue targets hybridize to complementary oligonucleotide probes under uniform hybridization conditions.

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35. A method of analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:

providing on a solid substrate an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences;

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exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under conditions effective to permit the plurality of oligonucleotide analogue probes to hybridize to complementary target oligonucleotides under uniform hybridization conditions; and

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determining whether an oligonucleotide analogue probe of said oligonucleotide probe array hybridizes to at least one of the oligonucleotide targets.

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36. A method of detecting an oligonucleotide target comprising:
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;

providing on a solid substrate an oligonucleotide array comprising a plurality of oligonucleotide probes selected to hybridize to complementary oligonucleotide analogue targets under uniform hybridization conditions;

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exposing the oligonucleotide analogue targets to the oligonucleotide array under conditions effective to permit the oligonucleotide probes to hybridize to complementary oligonucleotide analogue targets; and

detecting whether at least one of the oligonucleotide analogue targets hybridizes to a complementary oligonucleotide probe.

37. A method of making an array of oligonucleotide probes comprising;

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providing, on an array, a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue and different sequences, wherein the oligonucleotide analogue probes are selected to hybridize to complementary oligonucleotide targets under uniform hybridization conditions.

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